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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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FISH & RICHARDSON P.C.
3300 DAIN RAUSCHER PLAZA
60 SOUTH SIXTH STREET
MINNEAPOLIS, MN 55402

EXAMINER	
JOHANNSEN, DIANA B	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 07/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/826,581	ANDERSSON ET AL.	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-8,11-13 and 19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6-8,11-13 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

FINAL REJECTION

1. This action is in response to the Amendment and Reply filed April 4, 2003. Claims 1, 6-8, and 11-13 have been amended, claims 4-5, 9-10, and 14-18 have been canceled, and claim 19 has been added. Claims 1-3, 6-8, 11-13, and 19 are now pending and under consideration. The amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims. **This action is FINAL.**

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

3. In view of the cancellation of claims 4-5 and 9-10, the rejections of those claims under 35 U.S.C. 112, first paragraph are moot.

4. Claims 6-7, 12, and 19 are rejected under 35 U.S.C. 112, first paragraph, for the reasons set forth below and in the Office action of December 4, 2002. **It is noted that Applicant's amendments to the claims necessitated the inclusion of new claim 19 in this rejection.** Claim 19 is drawn to a nucleic acid comprising a variant at nucleotide 642; this position is located in intron 6 (which was recited in claim 10), and such nucleic acids were discussed in and encompassed by the rejection set forth in the Office action of December 4, 2002.

The response traverses the rejection on the following grounds. The response argues that the molecules of the claims "can be produced by standard techniques," that

the "sequence of human PRKAG3 is publically available in GenBank," and that specific point changes can be introduced into wild-type sequence using oligonucleotide-directed mutagenesis, polymerase chain reaction (PCR) techniques, or chemical synthesis." The response further urges that "Nucleic acids containing sequence variants at each of the recited positions can be used as probes and primers." The response states that "For example, as indicated at page 7 of the specification, such nucleic acid molecules can be specifically hybridized to a PCR product to determine if the product contains the variant nucleic acid sequence," and that "Such nucleic acid molecules can also be used to develop primers that can be used to amplify a product only when the variant allele is present."

These arguments have been thoroughly considered but are not persuasive. It is acknowledged that one of skill in the art could employ standard techniques to synthesize and/or isolate molecules meeting the requirements of the claims. However, 35 USC 112, first paragraph requires that the claimed invention be described in such a way as to enable one skilled in the art to both make and use the invention. As stated in *MPEP* 2164.07 regarding the enablement requirement, "35 U.S.C. 112, first paragraph requires an indication of how the use (required by 35 U.S.C. 101) can be carried out, i.e., how the invention can be used." Accordingly, to satisfy the enablement requirement, the combined teachings of the specification and the art must enable one of skill in the art to carry out a use that is specific, substantial, and credible (i.e., that meets the requirements of 35 USC 101). As discussed in the Office action of December 4, 2002, applicant has in fact asserted in the specification that the molecules of the claims

are useful in methods of detecting PRKAG3 variants associated with metabolic disorders, as well as in the production of polypeptides that are useful in such methods. Applicant has provided evidence of the existence of one such variant molecule (containing the C1037T polymorphism) that is associated with diabetes, and applicant's assertion that PRKAG3 variant nucleic acids may be detected as indicators of metabolic disorders is therefore a specific, substantial, and credible use. However, as discussed in the Office action of December 4, 2002, the combined teachings of the specification and the art do not provide evidence that the variants encompassed by the instant claims are actually associated with any metabolic disorders, and therefore it is unpredictable as to whether the claimed molecules could actually be used in the manner asserted by applicants without undue experimentation. While applicant argues that the molecules of the claims may be used as probes and/or primers to detect variant nucleic acid sequences by, e.g., hybridization or amplification methods, the teachings of the specification and of the art do not establish, e.g., an association between these variant molecules and metabolic disorders, as would be necessary to enable the use asserted by applicant that meets the criteria of 35 USC 101. Accordingly, applicant's arguments are not persuasive, and this rejection is maintained.

5. Claims 1-3, 8, and 11 are rejected under 35 U.S.C. 112, first paragraph, for the reasons set forth below and in the Office action of December 4, 2002.

The response notes that "Applicants have amended claim 1 to recite that the isolated nucleic acid includes a nucleotide sequence variant at a position selected from the group consisting of nucleotides 230, 559, 642, and 1037." The response again

argues (as discussed in the preceding paragraph) that "the specification provides guidance on how to make nucleic acid molecules that include a sequence variant," and that the specification "also provides guidance on using such nucleic acid molecules for probes and primers."

These arguments have been thoroughly considered but are not persuasive. It is acknowledged that claim 1 has been amended such that it refers to particular nucleotides. However, the claims as written are not clearly limited to, e.g., fragments of the recited SEQ ID Nos having a particularly length and including a disease-associated polymorphism, or to molecules that specifically detect a PRKAG3 molecule including such a particular variant nucleotide. Rather, the claims merely require an isolated nucleic acid comprising a particular nucleotide that is located at a specified position within a recited SEQ ID NO, flanked by any amount of flanking sequence, which isolated nucleic acid may include 15 or more base pairs. Accordingly, while the claims embrace a small number of molecules that would be useful in methods of diagnosing diabetes (e.g., those molecules that specifically detect the C1037T polymorphism, and/or which include a fragment of SEQ ID NO: 5 including the C1037T polymorphism and sufficient flanking sequence to effect specific detection), the claims also encompass a much larger number of molecules that would not be useful in such methods, and which differ both structurally and functionally from molecules that could used successfully in disease diagnosis. It is also noted again that, as discussed above, to satisfy the enablement requirement, the combined teachings of the specification and the art must enable one of skill in the art to carry out a use that is specific, substantial, and

credible. Accordingly, applicant's arguments are not persuasive, and this rejection is maintained.

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANT'S AMENDMENTS TO THE CLAIMS:

6. Claims 1-3, 6-8, 11-13, and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-3, 6-8, 11-13, and 19 are indefinite over the recitation of the phrase "wherein said nucleotide sequence variant is at a position selected from the group consisting of nucleotide 230 of SEQ ID NO:5, nucleotide 559 of SEQ ID NO:5, nucleotide 642 of SEQ ID NO:3, and nucleotide 1037 of SEQ ID NO:5" in claim 1. As the claims as written do not actually require, e.g., a molecule including any of the recited SEQ ID Nos, it is unclear as to how one could identify molecules meeting the requirements of the claims. For example, how would one differentiate a guanine that is a "variant" of a single position in a particular SEQ ID NO from any other guanine? It is further noted that the claim previously recites the limitation "wherein said human PRKAG3 sequence comprises a nucleotide sequence variant and nucleotides flanking said sequence variant." However, it is not clear from the language of the claims whether these recitations are referring to, e.g., flanking sequence located within the recited SEQ ID Nos, or to any type of PRKAG3 sequence flanking sequences. Clarification is required.

Claims 6-8 and 19 are indefinite because it is unclear as to how the claims further limit claim 1, from which they depend. It is noted that claim 1 is drawn to molecules comprising any 1 of 4 recited "nucleotide sequence variants." Claims 6-8 and 19 as written merely further limit the identity of one member of the group of claim 1, without actually including a requirement for a molecule that includes said variant. While it is clear how claim 6 would further limit claim 1 in the instances when claim 1 encompasses "nucleotide 230 of SEQ ID NO:5," it is unclear as to how or whether the claim would be further limiting of the 3 other types of variant encompassed thereby. As a proper dependent claim must further limit the claim from which it depends, claims 6-8 should be amended so as to, e.g., require a molecule that actually includes the variant whose properties are further limited by the claims.

Claims 12-13 are indefinite over the recitation of the phrase "wherein said amino acid sequence variant is a substitution of a ____ residue for a ____ residue at amino acid ___ of SEQ ID NO:6." As the claims as written do not actually require molecules that includes SEQ ID NO:6, it is unclear as to how one could identify molecules meeting the requirements of the claims. For example, with regard to claim 12, how would one identify an alanine that is a substitution "for a proline residue at amino acid 71 of SEQ ID NO:6" in a molecule that does not include SEQ ID NO:6? Clarification is required.

Claim Rejections - 35 USC § 102

7. In view of the cancellation of claims 4-5, the rejection of the claims under 35 U.S.C. 102(b) as being clearly anticipated by Cheung et al (The Biochemical Journal 346(Pt. 3):659-669 [March 2000]) is moot.

1. Claims 1 is rejected under 35 U.S.C. 102(b) as being clearly anticipated by Cheung et al (The Biochemical Journal 346(Pt. 3):659-669 [March 2000]), for the reasons set forth below and in the Office action of December 4, 2002.

The response traverses the rejection on the following grounds. The response states that "Claim 1 has been amended to recite that the isolated nucleic acid includes a nucleotide sequence variant at a position selected from the group consisting of nucleotide 230 of SEQ ID NO:5, nucleotide 559 of SEQ ID NO:5, nucleotide 642 of SEQ ID NO:3, and nucleotide 1037 of SEQ ID NO:5." The response argues that "The Cheung et al. reference does not disclose a sequence variant at the recited positions" and therefore does not anticipate claim 1.

This argument has been thoroughly considered but is not persuasive. As discussed above, the claim as written is not clearly limited to, e.g., fragments of the recited SEQ ID Nos having a particularly length and including a disease-associated polymorphism, or to molecules that specifically detect a PRKAG3 molecule including such a particular variant nucleotide. Rather, the claims merely require an isolated nucleic acid comprising a particular nucleotide that is located at a specified position within a recited SEQ ID NO (rather than, e.g., the entire SEQ ID NO, or a particular portion thereof), flanked by any amount of flanking sequence, which isolated nucleic acid includes 15 or more base pairs. The molecule of Cheung et al includes each of the nucleotides that are the "variant" nucleotides present at the particular SEQ ID NO locations recited in the claims, and the nucleotides of Cheung et al are flanked by

PRKAG3 sequences. Accordingly, Cheung et al anticipate the invention of claim 1, and this rejection is maintained.

Conclusion

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 703/305-0761. The examiner can normally be reached on Monday-Friday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached at 703/308-1152. The fax phone numbers

for the organization where this application or proceeding is assigned are 703/872-9306 for regular communications and 703/872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703/308-0196.

Diana B. Johannsen
July 3, 2003

CARLA J. MYERS
PRIMARY EXAMINER